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     (FILE 'HOME' ENTERED AT 11:16:13 ON 08 JUL 2002)

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 11:16:22 ON 08 JUL 2002
L1          8596 S (MOUSE? OR MURINE?) AND (HUMAN? OR MAN OR HOMO?) AND
(EXPRESS
L2          3436 S L1 AND (HOMOLOG?)
L3          2246 S (MOUSE? OR MURINE?) (P) (HUMAN? OR MAN OR HOMO?) (P)
(EXPRESS

     FILE 'MEDLINE' ENTERED AT 11:18:53 ON 08 JUL 2002
L4           725 S L3
L5             2 S L4 AND (CAG OR TRINUCLEOTIDE OR TRIPLET)
L6           421 S (MOUSE? OR MURINE?) (P) (HUMAN? OR MAN OR HOMOSAPEIN? OR
HOMO
L7             1 S L6 AND (TRINUCLEOTIDE? OR CAG OR TRIPLE?)
L8             3 S L6 AND (HUNTINGTON OR SPINOCEREBELLAR OR ATAXIA)
L9          2842 S (EXPRESS?) (P) (DIFFERENTIAL?) (P) HOMOLOG?
L10        78575 S (MOUSE? OR MURINE?) (P) (HUMAN? OR MAN OR HOMOSAPIEN? OR
HOM
L11       240718 S HOMLOGY? OR HOMOLOG?
L12      1401619 S DIFFERENT?
L13       687636 S EXPRESS?
L14          638 S L10 AND L11 AND (L12 (3A) L13)
L15          418 S L10 (P) L11 (P) (L12 (3A) L13)
L16          638 S (L10 (10A) L11 (10A) (L12 (3A) L13))
L17          638 S L10 (10A) L11 (10A) (L12 (3A) L13)
L18           61 S L11/TI AND L15

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L18 ANSWER 5 OF 61 MEDLINE
ACCESSION NUMBER: 2000330343 MEDLINE
DOCUMENT NUMBER: 20330343 PubMed ID: 10871356
TITLE: Analysis of uracil-DNA glycosylases from the **murine** Ung gene reveals **differential expression** in tissues and in embryonic development and a subcellular sorting pattern that differs from the **human homologues**.
AUTHOR: Nilsen H; Steinsbekk K S; Otterlei M; Slupphaug G; Aas P A;
Krokan H E
CORPORATE SOURCE: Institute for Cancer Research and Molecular Biology, Medical Faculty, Norwegian University of Science and Technology, N-7489 Trondheim, Norway.
SOURCE: NUCLEIC ACIDS RESEARCH, (2000 Jun 15) 28 (12) 2277-85. Journal code: 0411011. ISSN: 1362-4962.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF174485
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000810
Last Updated on STN: 20010521
Entered Medline: 20000727

AB The **murine** UNG: gene encodes both mitochondrial (Ung1) and nuclear (Ung2) forms of uracil-DNA glyco-sylase. The gene contains seven exons organised like the **human** counterpart. While the putative Ung1 promoter (P(B)) and the **human** P(B) contain essentially the same, although differently organised, transcription factor binding elements, the Ung2 promoter (P(A)) shows limited **homology** to the **human** counterpart. Transient transfection of chimaeric promoter-luciferase constructs demonstrated that both promoters are functional and that P(B) drives transcription more efficiently than P(A). mRNAs for Ung1 and Ung2 are found in all adult tissues analysed, but they are **differentially expressed**. Furthermore, transcription of both mRNA forms, particularly Ung2, is induced in mid-gestation embryos. Except for a strong conservation of the 26 N-terminal residues in Ung2, the subcellular targeting sequences in the encoded proteins have limited **homology**. Ung2 is transported exclusively to the nucleus in NIH 3T3 cells as expected. In contrast, Ung1 was sorted both to nuclei and mitochondria. These results demonstrate that although the catalytic domain of uracil-DNA glycosylase is highly conserved in **mouse** and **man**, regulatory elements in the gene and subcellular sorting sequences in the proteins differ both structurally and functionally, resulting in altered contribution of the isoforms to total uracil-DNA glycosylase activity.

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=> d ibib ab 1-19

L4 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:676917 CAPLUS
DOCUMENT NUMBER: 135:253736
TITLE: Human cyclic nucleotide phosphodiesterase that hydrolyzes both cAMP and cGMP
INVENTOR(S): Miyaji, Hiromasa; Haruoka, Motoko; Ota, Toshio; Kawabata, Ayako; Sugano, Sumio; Nakamura, Yusuke
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001066716	A1	20010913	WO 2001-JP1720	20010306

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2000-61464 A 20000307
JP 2000-208610 A 20000710

AB Novel cyclic nucleotide phosphodiesterase isoforms; cDNAs; recombinant expression; an antibody; immunoassay and immunostaining method by using this antibody; antisense oligonucleotides, promoter, and use in screening substances modifying the expression of the gene or the activity of the polypeptide; are disclosed. Use of the DNA of the novel PDE polypeptide in diagnosis, prevention and treatment of diabetes, ischemic heart diseases, hypertension, nephritis, pancreatitis, ulcer, allergy, asthma, rheumatism, osteoporosis, pain, anxiety, schizophrenia, manic-depressive psychosis, Parkinson's disease, dementia, infectious diseases, malignant tumor, etc., is claimed. CDNA encoding a novel phosphodiesterase (PDE) was isolated from a human HepG2 cell cDNA library. The deduced amino acid sequence contains 474 amino acids, and showed homol. to PDE5A and **PDE10A**. Recombinant enzyme transfected and expressed in E. coli cells hydrolyzed cAMP and cGMP. The transcripts were particularly abundant in pancreas. CDNA was also cloned from human fetal kidney cDNA library. This isoform showed high homol. to PDE5A. Tissue distribution in testis, prostate, mammary gland, and pancreas, was detected.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:265237 CAPLUS
DOCUMENT NUMBER: 134:305278
TITLE: Gene necessary for striatal function, uses thereof, and compounds for modulating same
INVENTOR(S): Robertson, Harold A.; Denovan-Wright, Eileen M.
PATENT ASSIGNEE(S): Novaneuron Inc., Can.

SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001024781	A2	20010412	WO 2000-CA1188	20001006
WO 2001024781	A3	20020207		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: CA 1999-2285690 A 19991007
US 1999-158043P P 19991007
US 2000-217765P P 20000712

AB **PDE10A**, a gene that is normally highly expressed in mammalian striatum and elsewhere, has been found to decrease in expression during the development of CAG repeat disorders such as Huntington's disease. The invention teaches a method for detecting the presence of or the predisposition for a CAG repeat disorder. Compds. which modulate CAG repeat disorders and their uses are taught. Methods for screening for further compds. to modulate CAG repeat disorders are also taught.

L4 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:444371 CAPLUS
DOCUMENT NUMBER: 135:57850
TITLE: Human cyclic nucleotide phosphodiesterase that hydrolyzes both cAMP and cGMP (**PDE10A**)
INVENTOR(S): Tanaka, Toshio
PATENT ASSIGNEE(S): Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 32 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001161379	A2	20010619	JP 2000-297366	20000928

PRIORITY APPLN. INFO.: JP 1999-276957 A 19990929

AB A new cyclic nucleotide phosphodiesterase isoform **PDE10A**, recombinant expression, antibodies, and screening of ligands or regulators, are disclosed. Cloning Sf9 cells. CDNA encoding a novel phosphodiesterase (PDE) was isolated from a human fetal lung cDNA library and designated **PDE10A**. The deduced amino acid sequence contains 779 amino acids, including a putative cGMP binding sequence in the amino-terminal portion of the mol. and a catalytic domain that is 16-47% identical in amino acid sequence to those of other PDE families. Recombinant **PDE10A** transfected and expressed in COS-7 cells hydrolyzed cAMP and cGMP with Km values of 0.26 and 7.2 .mu.M, resp., and

Vmax with cGMP was almost twice that with cAMP. Of the PDE inhibitors tested, dipyridamole was most effective, with IC50 values of 1.2 and 0.45 .mu.M for inhibition of cAMP and cGMP hydrolysis, resp. CGMP inhibited hydrolysis of cAMP, and cAMP inhibited cGMP hydrolysis with IC50 values of 14 and 0.39 .mu.M, resp. Thus, **PDE10A** exhibited properties of a cAMP PDE and a cAMP-inhibited cGMP PDE. **PDE10A** transcripts were particularly abundant in the putamen and caudate nucleus regions of brain and in thyroid and testis, and in much lower amts. in other tissues. The PDE10OA gene was located on chromosome 6q26 by fluorescent in situ hybridization anal. **PDE10A** represents a new member of the PDE superfamily, exhibiting unique kinetic properties and inhibitor sensitivity.

L4 ANSWER 4 OF 19 MEDLINE
ACCESSION NUMBER: 2001555324 MEDLINE
DOCUMENT NUMBER: 21488127 PubMed ID: 11602184
TITLE: The gamma subunit of the rod photoreceptor cGMP phosphodiesterase can modulate the proteolysis of two cGMP binding cGMP-specific phosphodiesterases (PDE6 and PDE5) by caspase-3.
AUTHOR: Frame M; Wan K F; Tate R; Vandenabeele P; Pyne N J
CORPORATE SOURCE: Department of Physiology and Pharmacology, Strathclyde Institute for Biomedical Sciences, University of Strathclyde, 27 Taylor Street, Glasgow G4 ONR, UK.
SOURCE: CELLULAR SIGNALLING, (2001 Oct) 13 (10) 735-41. Journal code: 8904683. ISSN: 0898-6568.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF190928
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011017
Last Updated on STN: 20020122
Entered Medline: 20011204

AB We have investigated whether the proteolysis of members of the cGMP binding phosphodiesterases (PDE6, PDE5A1, and PDE10A2) by caspase-3 is modulated by the gamma inhibitor subunit of PDE6. We show here that purified caspase-3 proteolyses PDE6, an enzyme composed of two nonidentical catalytic subunits (termed alpha and beta) with molecular mass of 88 and 84 kDa. The proteolysis of PDE6 produced a single fragment with a molecular mass of 78 kDa. This corresponds to the possible cleavage of the caspase-3 consensus DFVD site (amino acids: 164-168) in the alpha subunit and leads to a 50% decrease in the cGMP hydrolysing activity of the enzyme. The addition of rod PDEgamma to the incubation completely blocked the cleavage of PDE6 by caspase-3. In contrast, rod PDEgamma converted PDE5A1 (molecular mass of 98 kDa) to a better substrate for caspase-3. This resulted in the formation of four major fragments with molecular mass of 82-83, 67, 43, and 34 kDa. In addition, caspase-3 induced an approximately 80% reduction in the activity of a partially purified preparation of PDE5A1 in the presence of rod PDEgamma. Caspase-3 also cleaved PDE10A2 (molecular mass of 95 kDa) to a single 48-kDa fragment. This was consistent with cleavage of the DLFD site (amino acids: 312-315) in PDE10A2. In contrast with both PDE6 and PDE5A1, rod PDEgamma was without effect on this enzyme. These data show that rod PDEgamma interacts with at least two members of the cGMP binding PDE family (PDE5A1

and PDE6) and can exert differential effects on the cleavage of these enzymes by caspase-3.

L4 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:507091 CAPLUS
DOCUMENT NUMBER: 136:178643
TITLE: A set of 840 mouse oocyte genes with well-matched human homologs
AUTHOR(S): Stanton, J. L.; Green, D. P. L.
CORPORATE SOURCE: Department of Anatomy and Structural Biology, Medical School, University of Otago, Dunedin, N. Z.
SOURCE: Molecular Human Reproduction (2001), 7(6), 521-543
CODEN: MHREFD; ISSN: 1360-9947
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB GenBank contains 14,477 expressed sequence tags (EST) derived from mouse oocyte cDNA libraries: 3499 of these are from two unfertilized oocyte libraries and 10,978 are from two fertilized oocyte libraries. Gene expression profiles were obtained for these libraries by matching library EST to UniGene clusters. The 14,477 EST identified 4226 UniGenes. These were screened using HomoloGene to identify 1386 homologous UniGene clusters in two other species with one of the matches being human. Within these human matches, 840 encoded named proteins, 223 encoded hypothetical proteins, and 323 encoded clustered EST. The set of named genes provides the first step in establishing a database of genes expressed in mouse oocytes and, by extension, human oocytes.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 19 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001108293 MEDLINE
DOCUMENT NUMBER: 20570133 PubMed ID: 11121118
TITLE: Genomic organization of the human phosphodiesterase PDE11A gene. Evolutionary relatedness with other PDEs containing GAF domains.
AUTHOR: Yuasa K; Kanoh Y; Okumura K; Omori K
CORPORATE SOURCE: Discovery Research Laboratory, Tanabe Seiyaku Co. Ltd, Toda, Saitama, Japan.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (2001 Jan) 268 (1) 168-78.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB048401; GENBANK-AB048402; GENBANK-AB048403; GENBANK-AB048404; GENBANK-AB048405; GENBANK-AB048406; GENBANK-AB048407; GENBANK-AB048408; GENBANK-AB048409; GENBANK-AB048410; GENBANK-AB048411; GENBANK-AB048412; GENBANK-AB048413; GENBANK-AB048414; GENBANK-AB048415; GENBANK-AB048416; GENBANK-AB048417; GENBANK-AB048418; GENBANK-AB048419; GENBANK-AB048420; GENBANK-AB048421; GENBANK-AB048422; GENBANK-AB048423
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322

Entered Medline: 20010208

AB PDE11A is a dual-substrate, cAMP and cGMP, cyclic nucleotide phosphodiesterase (PDE). Presently four unique variants carrying distinct GAF sequences in the N-terminal region have been identified. While human PDE11A3 and PDE11A4 are known to be specifically expressed in testis and prostate, respectively, PDE11A1 was mainly detected in skeletal muscle. The human PDE11A gene was investigated and revealed to span > 300 kb, contain 23 exons and be mapped on chromosome 2q31. The transcription start sites of PDE11A1, PDE11A3 and PDE11A4 were determined, and the promoter sequences were revealed. Although 5' flanking genomic regions of PDE11A1 and PDE11A3 had a consensus TATA motif, that of PDE11A4 was a TATA-less but contained CCAAT box and Sp1-binding sequence. Interestingly, we found that the exon 2 sequence for N-terminal region of PDE11A3 encoded an N-terminal sequence of the cytochrome c pseudogene in an alternate reading frame, and that C-terminal region of the cytochrome c pseudogene in intron 2 was disrupted by the insertion of Alu repetitive sequence. Furthermore, we examined the exon-intron organization of the PDE2A gene and compared the exon organization among GAF-PDE family. The exon organization of the PDE11A catalytic domain was very similar to those of PDE5A and PDE6B. However, other GAF-PDEs, PDE2A and **PDE10A**, displayed different exon organization from PDE11A although these three PDEs are similar in their amino-acid sequences to each other. The findings suggested that PDE11A has a common ancestral gene with PDE5A and PDE6s, whereas PDE2A and **PDE10A** are generated separately from these three GAF-PDEs.

L4 ANSWER 7 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:487012 BIOSIS
DOCUMENT NUMBER: PREV200100487012
TITLE: Distribution of neurons expressing the **PDE10A** mRNA in the rat brain.
AUTHOR(S): Morita, Y. (1); Hosokawa, N. (1); Hayashi, Y.; Murayama, N.
CORPORATE SOURCE: (1) Anatomy and Physiology, Kagawa Prefectural College of Health Sciences School of Medical Technology, Kagawa Japan
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 105. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Of 11 families of PDE genes, **PDE10A** has been recently cloned and characterized as exhibiting properties of a cGMP-binding cAMP-specific PDE and a cAMP-inhibited cGMP-PDE in humans and rodents. **PDE10A** can hydrolyze both cAMP and cGMP functioning as second messengers in intracellular signaling. Splice variants of the **PDE10A** mRNA are reported in human and rodents, implying functional differences between them. In this study gene expression of **PDE10A** in the rat brain was examined by dot blot hybridization, Northern blot analysis, and in situ hybridization using synthetic oligonucleotide probes, corresponding to the sequence of the catalytic domain of **PDE10A**. In Northern blot analysis, the striatum showed a clear signal of more than 8,100 base-sized mRNA, while other brain tissues failed to show an identical

band of target mRNA clearly. Dot blot hybridization, however, showed signals in various brain tissues with different intensity. Striatum showed a relatively strong signal, followed by the cerebral cortex, and relatively low signals in the cerebellum, hippocampus and olfactory bulb and tubercle. Using in situ hybridization, neurons expressing **PDE10A** mRNA were observed in various brain regions. Substantial numbers of positive neurons were found in the striatum, cerebral cortex and cerebellum. A small number of positive neurons were located in central olfactory structures, nucleus accumbens, hippocampal formation, thalamus (lateral nuclei), and amygdaloid complex. A few positive neurons were seen in other brain regions as well.

L4 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:475804 CAPLUS
DOCUMENT NUMBER: 133:100483
TITLE: Human cyclic nucleotide phosphodiesterase isoforms and their encoding nucleic acids
INVENTOR(S): Phillips, Stephen C.; Lanfear, Jerry; Fawcett, Lindsay; Bandman, Olga; Harrow, Ian
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040733	A1	20000713	WO 2000-US371	20000107
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6100037	A	20000808	US 1999-226741	19990107
EP 1141332	A1	20011010	EP 2000-905560	20000107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-226741 A2 19990107
WO 2000-US371 W 20000107

AB The invention provides human cyclic nucleotide phosphodiesterases (HSPDE10A) and polynucleotides which identify and encode HSPDE10A. Nucleic acids encoding HSPDE10A were identified in Incyte clone 826776 from a human prostate cDNA library and used to obtain full-length cDNA sequences from a human skeletal muscle library. HSPDE10A1 is 490 amino acids in length and has a putative cGMP binding motif and a PDE signature motif, and has chem. and structural similarity with human PDE5. A C-terminal splice variant, HSPDE10A2, is 367 amino acids in length and contains the same cGMP binding and PDE motifs. Northern anal. showed that HSPDE10A is expressed in skeletal muscle and prostate as a major

transcript of .apprx.7.5 kb; a .apprx.3.0 kb mRNA was detected only in prostate; and a less prominent transcript of .apprx.1.5 kb occurred in testes and skeletal muscle. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders assocd. with expression of HSPDE10A.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:562643 CAPLUS
DOCUMENT NUMBER: 133:173997
TITLE: Novel phosphodiesterase that hydrolyzes both cAMP and cGMP (**PDE10A** and PDE10A2) from human and (PDE10A2 and PDE10A3) from rat, genes, recombinant expression, and uses
INVENTOR(S): Omori, Kenji; Odera, Atsushi; Fujie, Kotomi; Michibata, Hideo; Yuasa, Keizo
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 29 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000224992	A2	20000815	JP 1999-129343	19990511

PRIORITY APPLN. INFO.: JP 1998-338861 A 19981130

AB A novel type 10 phosphodiesterases (PDE10) from human and rat catalyzing the hydrolysis of cyclic nucleotides, their genes, recombinant expression, and methods of characterizing, identifying, or selecting their inhibitors, are disclosed. A method of detecting those genes using primers and probes, and of detecting the expression of those genes in tissues using antibodies, are also claimed. CDNA encoding a novel phosphodiesterase (PDE) was isolated from a human fetal lung cDNA library and designated **PDE10A**. The deduced amino acid sequence contains 779 amino acids, including a putative cGMP binding sequence in the amino-terminal portion of the mol. and a catalytic domain that is 16-47% identical in amino acid sequence to those of other PDE families. Recombinant **PDE10A** transfected and expressed in COS-7 cells hydrolyzed cAMP and cGMP with Km values of 0.26 and 7.2 .mu.M, resp., and Vmax with cGMP was almost twice that with cAMP. Of the PDE inhibitors tested, dipyridamole was most effective, with IC50 values of 1.2 and 0.45 .mu.M for inhibition of cAMP and cGMP hydrolysis, resp. CGMP inhibited hydrolysis of cAMP, and cAMP inhibited cGMP hydrolysis with IC50 values of 14 and 0.39 .mu.M, resp. Thus, **PDE10A** exhibited properties of a cAMP PDE and a cAMP-inhibited cGMP PDE. **PDE10A** transcripts were particularly abundant in the putamen and caudate nucleus regions of brain and in thyroid and testis, and in much lower amts. in other tissues. **PDE10A** represents a new member of the PDE superfamily, exhibiting unique kinetic properties and inhibitor sensitivity. A novel alternative splice variant of human cAMP- and cGMP-hydrolyzing phosphodiesterase (PDE10A2) was also isolated from human fetal lung. The N-terminal sequence of human PDE10A2 differed from that of human PDE10A1 reported

previously. PDE10A1 and PDE10A2 expressed in COS-7 cells have cGMP Km values of 14 and 13 .mu.M, low cAMP Km values of 0.28 and 0.22 .mu.M, and high cAMP Km values of 0.96 and 1.1 .mu.M, resp., at high concns. of cGMP and cAMP. PCR anal. demonstrated that both PDE10A1 and PDE10A2 transcripts are present in various human tissues and that PDE10A2 transcripts are a major form in some human tissues. The unique N-terminus of PDE10A2 has a putative phosphorylation site by cAMP-dependent protein kinase (cAK), but PDE10A1 does not. The recombinant PDE10A2 protein is preferentially phosphorylated by cAK, although the recombinant PDE10A1 protein is not phosphorylated by cAK. Two splicing variants of a phosphodiesterase (PDE10A2 and PDE10A3) exhibiting properties of a cAMP PDE and a cAMP-inhibited cGMP PDE, were also isolated from rat and cDNAs cloned. PDE10A2 and PDE10A3 transcripts were abundant in the brain and testis. In situ hybridization anal. using a **PDE10A** riboprobe demonstrated the presence of **PDE10A** transcripts in the neurons of the striatum and the olfactory tubercle regions of the brain. Rat **PDE10A** cDNAs were isolated from a brain cDNA library and nucleotide sequence anal. revealed several N-terminal variants. The deduced amino-acid sequence of one of the major variant forms contained 794 amino acids, and it was 96% identical to that of the human PDE10A2. The other major form has a distinct N-terminal sequence that is not found in humans. **PDE10A** was partially purified from rat striatum and testis, and characterized with respect to Km, inhibitor sensitivity and immunoreactivity to an anti-**PDE10A** serum. These findings indicate that **PDE10A** functions in these tissues.

L4 ANSWER 10 OF 19 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2000:534352 SCISEARCH
THE GENUINE ARTICLE: 332QG
TITLE: Multiple zinc binding sites in retinal rod cGMP phosphodiesterase, PDE6 alpha beta
AUTHOR: He F; Seryshev A B; Cowan C W; Wensel T G (Reprint)
CORPORATE SOURCE: BAYLOR COLL MED, DEPT BIOCHEM, 1 BAYLOR PLAZA, HOUSTON, TX 77030 (Reprint); BAYLOR COLL MED, VERNA & MARRS MCLEAN DEPT BIOCHEM & MOL BIOL, HOUSTON, TX 77030
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (7 JUL 2000) Vol. 275, No. 27, pp. 20572-20577.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 35

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The photoreceptor cGMP phosphodiesterase (PDE6) plays a key role in vertebrate vision, but its enzymatic mechanism and the roles of metal ion co-factors have yet to be determined. We have determined the amount of endogenous Zn2+ in rod PDE6 and established a requirement for tightly bound Zn2+ in catalysis, Purified PDE6 contained 3-4-g atoms of zinc/mole, consistent with an initial content of two tightly bound Zn2+/catalytic subunit. PDE with only tightly bound Zn2+ and no free metal ions was inactive, but activity was fully restored by Mg2+, Mn2+, Co2+, or Zn2+. Mn2+, Co2+, and Zn2+ also induced aggregation and inactivation at higher concentrations and longer times. Removal of 93% of the tightly bound Zn2+ by treatment with dipicolinic acid and EDTA at pH 6.0 resulted in almost

complete loss of activity in the presence of Mg2+. This activity loss was blocked almost completely by Zn2+, less potently by Co2+ and almost not at all by Mg2+, Mn2+, or Cu2+. The lost activity was restored by the addition of Zn2+, but Co2+ restored only 13% as much activity, and other metals even less. Thus tightly bound Zn2+ is required for catalysis but could also play a role in stabilizing the structure of PDE6, whereas distinct sites where Zn2+ is rapidly exchanged are likely occupied by Mg2+ under physiological conditions.

L4 ANSWER 11 OF 19 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001026933 MEDLINE
DOCUMENT NUMBER: 20453115 PubMed ID: 10998054
TITLE: The human phosphodiesterase **PDE10A** gene genomic organization and evolutionary relatedness with other PDEs containing GAF domains.
AUTHOR: Fujishige K; Kotera J; Yuasa K; Omori K
CORPORATE SOURCE: Discovery Research Laboratory, Tanabe Seiyaku Co. Ltd, Saitama, Japan.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (2000 Oct) 267 (19) 5943-51.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001113

AB **PDE10A** is a cyclic nucleotide phosphodiesterase (PDE) exhibiting properties of a cAMP PDE and a cAMP-inhibited cGMP PDE. The transcripts are specifically expressed in the striatum. The human gene encoding **PDE10A** was cloned and investigated. The **PDE10A** gene spanned > 200 kb and contained 24 exons. The exon-intron organization of **PDE10A** was different from those of PDE5A and PDE6B, although these three PDEs include two GAF domains and have similar amino-acid sequences. The promoter sequence of **PDE10A** was highly GC-rich and did not contain a TATA motif and a CAAT box, suggesting it is a housekeeping gene.

In Caenorhabditis elegans, the C32E12.2 gene encoding a probable PDE that is 48% identical to the human **PDE10A** protein showed similar exon organization to **PDE10A** but not PDE5A and PDE6B. This, together with the phylogenic tree analysis, suggested that the ancestral gene for **PDE10A** existed in a lower organism such as C. elegans.

L4 ANSWER 12 OF 19 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2000:629980 SCISEARCH
THE GENUINE ARTICLE: 343BP
TITLE: Rabbit corpus cavernosum smooth muscle shows a different phosphodiesterase profile than human corpus cavernosum
AUTHOR: Qiu Y H (Reprint); Kraft P; Lombardi E; Clancy J
CORPORATE SOURCE: RW JOHNSON PHARMACEUT RES INST, DEPT REPROD THERAPEUT, 1000 ROUTE 202 S, RARITAN, NJ 08869 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF UROLOGY, (SEP 2000) Vol. 164, No. 3, Part 1, pp. 882-886.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.

ISSN: 0022-5347.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Purpose: Cyclic nucleotide phosphodiesterases (PDEs) are important regulators of cAMP/cGMP secondary messenger systems. Fluctuations in the level of cyclic nucleotides control the smooth muscle tone of corpus cavernosum. It had been shown that milrinone, a PDE3 inhibitor, was as potent as sildenafil, a PDE5 inhibitor, in relaxing human corpus cavernosum. However, milrinone is much less effective in relaxing rabbit corpus cavernosum than sildenafil. PDEs in rabbit corpus cavernosum were characterized and organ bath experiments were carried out in an attempt to search for the biochemical basis of this species difference.

Materials and Methods: In a biochemical study, PDE isozymes from rabbit corpus cavernosum were isolated by FPLC and characterized by PDE assay. In organ bath experiments, rabbit corpus cavernous tissue strips were precontracted and increasing doses of various inhibitors were added.

Results: The major PDE in rabbit corpus cavernosum is PDE5. There are small amounts of PDE2 and PDE1. PDE3, which contributes significantly to the total PDE activity in human corpus cavernosum, is apparently lacking in rabbit corpus cavernosum. Organ bath experiments with isotype-specific inhibitors confirm this conclusion.

Conclusion: The distribution of PDE isozymes in corpus cavernosum is different in human and in rabbit. This could be the biochemical basis for the differential effects of milrinone in relaxing rabbit and human corpus cavernosum. Our study emphasizes the importance of a more complete understanding of the tissue distribution of targeted proteins in an animal model before applying the results to humans.

L4 ANSWER 13 OF 19 MEDLINE
ACCESSION NUMBER: 2000179485 MEDLINE
DOCUMENT NUMBER: 20179485 PubMed ID: 10712916
TITLE: Regulation of cAMP and cGMP signaling: new phosphodiesterases and new functions.
AUTHOR: Soderling S H; Beavo J A
CORPORATE SOURCE: Department of Pharmacology, Box 357280, University of Washington, Seattle 98195, USA.
CONTRACT NUMBER: DK2173 (NIDDK)
HL4498 (NHLBI)
HL60178 (NHLBI)
SOURCE: CURRENT OPINION IN CELL BIOLOGY, (2000 Apr) 12 (2) 174-9.
Ref: 41
Journal code: 8913428. ISSN: 0955-0674.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000525
Last Updated on STN: 20000525
Entered Medline: 20000512

AB The past eighteen months have provided much progress in the cyclic

nucleotide phosphodiesterase (PDE) field. Six new phosphodiesterase genes have been discovered and characterized. In addition, several new highly specific PDE inhibitors have been developed and approved for clinical use.

Finally, new strategies have been employed to determine PDE function in model systems including the use of antisense oligonucleotide and disruption techniques.

L4 ANSWER 14 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:96813 BIOSIS
DOCUMENT NUMBER: PREV200100096813
TITLE: **PDE10A** mRNA in situ hybridization mapping in the rodent brain: apparent co-localization with dopaminoceptive neurons.
AUTHOR(S): Seeger, T. F. (1); Wylie, P. G.
CORPORATE SOURCE: (1) Pfizer Central Research, Groton, CT USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-345.10. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Whole brain expression mapping of phosphodiesterase 10A (**PDE10A**) mRNA in mouse and rat brain was accomplished using in situ hybridization autoradiography. **PDE10A** message has a highly specific distribution, with high expression levels seen only in striatum, nucleus accumbens and olfactory tubercle. Among the phosphodiesterases, it is most similar to the expression map previously described for PDE1B. Low levels of expression are seen in hippocampus (CA layers and dentate gyrus), cerebellum, and medial and sulcal prefrontal cortex. Emulsion autoradiographs show that PDE10 mRNA is expressed in the great majority of intrinsic striatal neurons. The **PDE10A** mRNA distribution pattern is strikingly similar to that of post-synaptic D1 and D2 dopamine receptors, and suggests that PDE10 is contained in the dopaminoceptive medium spiny neurons. The **PDE10A** enzyme may therefore play a key role in modulating the functional consequences of dopamine receptor activation.

L4 ANSWER 15 OF 19 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999303608 MEDLINE
DOCUMENT NUMBER: 99303608 PubMed ID: 10373451
TITLE: Cloning and characterization of a novel human phosphodiesterase that hydrolyzes both cAMP and cGMP (**PDE10A**).
AUTHOR: Fujishige K; Kotera J; Michibata H; Yuasa K; Takebayashi S;
Okumura K; Omori K
CORPORATE SOURCE: Discovery Research Laboratory, Tanabe Seiyaku Co. Ltd., 2-50, Kawagishi-2-chome, Toda, Saitama 335-8505, Japan.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Jun 25) 274 (26) 18438-45.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB020593
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990727
Last Updated on STN: 19990727
Entered Medline: 19990715

AB cDNA encoding a novel phosphodiesterase (PDE) was isolated from a human fetal lung cDNA library and designated **PDE10A**. The deduced amino acid sequence contains 779 amino acids, including a putative cGMP binding sequence in the amino-terminal portion of the molecule and a catalytic domain that is 16-47% identical in amino acid sequence to those of other PDE families. Recombinant **PDE10A** transfected and expressed in COS-7 cells hydrolyzed cAMP and cGMP with Km values of 0.26 and 7.2 microM, respectively, and Vmax with cGMP was almost twice that with cAMP. Of the PDE inhibitors tested, dipyridamole was most effective, with IC50 values of 1.2 and 0.45 microM for inhibition of cAMP and cGMP hydrolysis, respectively. cGMP inhibited hydrolysis of cAMP, and cAMP inhibited cGMP hydrolysis with IC50 values of 14 and 0.39 microM, respectively. Thus, **PDE10A** exhibited properties of a cAMP PDE and a cAMP-inhibited cGMP PDE. **PDE10A** transcripts were particularly abundant in the putamen and caudate nucleus regions of brain and in thyroid and testis, and in much lower amounts in other tissues. The **PDE10A** gene was located on chromosome 6q26 by fluorescent in situ hybridization analysis. **PDE10A** represents a new member of the PDE superfamily, exhibiting unique kinetic properties and inhibitor sensitivity.

L4 ANSWER 16 OF 19 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999289599 MEDLINE
DOCUMENT NUMBER: 99289599 PubMed ID: 10359840
TITLE: Isolation and characterization of a dual-substrate phosphodiesterase gene family: **PDE10A**.
AUTHOR: Soderling S H; Bayuga S J; Beavo J A
CORPORATE SOURCE: Department of Pharmacology, Box 357280, University of Washington, Seattle, WA 98195, USA.
CONTRACT NUMBER: DK21723 (NIDDK)
GM07750 (NIGMS)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Jun 8) 96 (12) 7071-6.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF110507
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990715
Last Updated on STN: 19990715
Entered Medline: 19990708

AB We report here the cloning, expression, and characterization of a dual-substrate, cAMP and cGMP, cyclic nucleotide phosphodiesterase (PDE) from mouse. This PDE contains the consensus sequence for a PDE catalytic domain, but shares <50% sequence identity with the catalytic domains of all other known PDEs and, therefore, represents a new PDE gene family, designated **PDE10A**. The cDNA for **PDE10A** is 3, 370 nt in length. It includes a full ORF, contains three in-frame stop codons upstream of the first methionine, and is predicted to encode a 779-aa enzyme. At the N terminus **PDE10A** has two GAF domains homologous to many signaling molecules, including PDE2, PDE5, and PDE6, which likely constitute a low-affinity binding site for cGMP. **PDE10A**

hydrolyzes cAMP with a Km of 0.05 microM and cGMP with a Km of 3 microM. Although **PDE10A** has a lower Km for cAMP, the Vmax ratio (cGMP/cAMP) is 4.7. RNA distribution studies indicate that **PDE10A** is expressed at highest levels in testis and brain.

L4 ANSWER 17 OF 19 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2000050627 MEDLINE
DOCUMENT NUMBER: 20050627 PubMed ID: 10583409
TITLE: Striatum- and testis-specific phosphodiesterase **PDE10A** isolation and characterization of a rat **PDE10A**.
AUTHOR: Fujishige K; Kotera J; Omori K
CORPORATE SOURCE: Discovery Research Laboratory, Tanabe Seiyaku Co. Ltd. Saitama, Japan.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1999 Dec) 266 (3) 1118-27.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB027155; GENBANK-AB027156
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000209
Last Updated on STN: 20000209
Entered Medline: 20000131

AB **PDE10A**, a phosphodiesterase (PDE) exhibiting properties of a cAMP PDE and a cAMP-inhibited cGMP PDE, was cloned and investigated in detail in rats. **PDE10A** transcripts were abundant in the brain and testis. In situ hybridization analysis using a **PDE10A** riboprobe demonstrated the presence of **PDE10A** transcripts in the neurons of the striatum and the olfactory tubercle regions of the brain. Rat **PDE10A** cDNAs were isolated from a brain cDNA library and nucleotide sequence analysis revealed several N-terminal variants. The deduced amino-acid sequence of one of the major variant forms contained 794 amino acids, and it was 96% identical to that of the human PDE10A2. The other major form has a distinct N-terminal sequence that is not found in humans. **PDE10A** was partially purified from rat striatum and testis, and characterized with respect to Km, inhibitor sensitivity and immunoreactivity to an anti-**PDE10A** serum. These findings indicate that **PDE10A** functions in these tissues.

L4 ANSWER 18 OF 19 MEDLINE
ACCESSION NUMBER: 1999373117 MEDLINE
DOCUMENT NUMBER: 99373117 PubMed ID: 10441464
TITLE: Characterization and phosphorylation of PDE10A2, a novel alternative splice variant of human phosphodiesterase that hydrolyzes cAMP and cGMP.
AUTHOR: Kotera J; Fujishige K; Yuasa K; Omori K
CORPORATE SOURCE: Discovery Research Laboratory, Tanabe Seiyaku Co. Ltd., 2-50, Kawagishi-2-chome, Toda, Saitama, 335-8505, Japan.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1999 Aug 11) 261 (3) 551-7.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB026816
ENTRY MONTH: 199909

ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 19990925
Entered Medline: 19990909

AB We have isolated a novel alternative splice variant of human cAMP- and cGMP-hydrolyzing phosphodiesterase (PDE10A2) from human fetal lung. The N-terminal sequence of human PDE10A2 differed from that of human PDE10A1 reported previously. PDE10A1 and PDE10A2 expressed in COS-7 cells have cGMP K(m) values of 14 and 13 microM, low cAMP K(m) values of 0.28 and 0.22 microM, and high cAMP K(m) values of 0.96 and 1.1 microM, respectively, at high concentrations of cGMP and cAMP. PCR analysis demonstrated that both PDE10A1 and PDE10A2 transcripts are present in various human tissues and that PDE10A2 transcripts are a major form in some human tissues. The unique N-terminus of PDE10A2 has a putative phosphorylation site by cAMP-dependent protein kinase (cAK), but PDE10A1 does not. The recombinant PDE10A2 protein is preferentially phosphorylated by cAK, although the recombinant PDE10A1 protein is not phosphorylated by cAK.

L4 ANSWER 19 OF 19 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1999321805 MEDLINE
DOCUMENT NUMBER: 99321805 PubMed ID: 10393245
TITLE: Isolation and characterization of **PDE10A**, a novel human 3', 5'-cyclic nucleotide phosphodiesterase.
AUTHOR: Loughney K; Snyder P B; Uher L; Rosman G J; Ferguson K; Florio V A
CORPORATE SOURCE: ICOS Corporation, Bothell, WA 98021, USA.. kloughney@icos.com
SOURCE: GENE, (1999 Jun 24) 234 (1) 109-17.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF127479; GENBANK-AF127480
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990819

AB A gene encoding a novel human 3', 5'-cyclic nucleotide phosphodiesterase (PDE) was identified and characterized. PDE10A1 encodes a protein that is 779 amino acids in length. An incomplete cDNA for a second 5'-splice variant, PDE10A2, was isolated. The proteins encoded by the two variants share 766 amino acids in common. This common region includes an amino-terminal domain with partial homology to the cGMP-binding domains of PDE2, PDE5 and PDE6 as well as a carboxy-terminal region with homology to the catalytic regions of mammalian PDEs. Northern analysis revealed that **PDE10A** is widely expressed. The **PDE10A** gene was mapped to three yeast artificial chromosomes (YACs) that contain human DNA from chromosome 6q26-27. A recombinant protein corresponding to the 766 amino acid region common to PDE10A1 and PDE10A2 was expressed in yeast. It hydrolyzed both cAMP and cGMP. Inhibitors that are selective for other PDE families are poor inhibitors of **PDE10A**; however, **PDE10A** is inhibited by the non-specific PDE inhibitor, IBMX.

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